

10/009930

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PASSWORD:

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SYSTEM LOGOFF AT 15:52:11 ON 23 JUL 2003 US EASTERN TIME

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PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' AT 15:52:35 ON 23 JUL 2003
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FILE 'EMBASE' ENTERED AT 15:52:35 ON 23 JUL 2003
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FILE 'BIOTECHDS' ENTERED AT 15:52:35 ON 23 JUL 2003
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.38	24.59

=> d his

(FILE 'HOME' ENTERED AT 15:41:55 ON 23 JUL 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003

E HARDER ACHIM/AU

L1 139 S E3

E VON SAMSON-HIMMELSTJERNA GEORG/AU

L2 2 S E4

=> e von samson georg/au

E1 34 VON SAMSON E/AU

E2 1 VON SAMSON G/AU

E3 0 --> VON SAMSON GEORG/AU

E4 1 VON SAMSON H/AU

E5 1 VON SAMSON HIMELSTJERNA G/AU

E6 1 VON SAMSON HIMELSTJERNA GEORG/AU

E7 1 VON SAMSON HIMMEL ST JERNA G/AU

E8 1 VON SAMSON HIMMELSRJEMA G/AU

E9 1 VON SAMSON HIMMELST JERNA G/AU

E10 1 VON SAMSON HIMMELSTJERNA A/AU

E11 101 VON SAMSON HIMMELSTJERNA G/AU

E12 45 VON SAMSON HIMMELSTJERNA GEORG/AU

=> e

E13 3 VON SAMSON HIMMELSTJERNA H O/AU

E14 7 VON SAMSON HIMMELSTJERNA M/AU

E15 3 VON SAMSON HIMMELSTJERNA M C/AU

E16 4 VON SAMSON HIMMELSTJERNA MATTHIAS/AU

E17 1 VON SAMSON HIMMESTJERNA M/AU

E18 1 VON SAMSON HIMMESTJERNA MATTHIAS/AU

E19 2 VON SAMSON JOERG/AU

E20 7 VON SAMSON P/AU

E21 7 VON SAMSON PATRICK/AU

E22 1 VON SAMSON V E/AU

E23 2 VON SAMSONHIMMELSTJERNA G/AU

E24 1 VON SAMSONOW ALEXANDER/AU

=> s e2-e12

L3 149 ("VON SAMSON G"/AU OR "VON SAMSON GEORG"/AU OR "VON SAMSON H"/AU OR "VON SAMSON HIMELSTJERNA G"/AU OR "VON SAMSON HIMELSTJERNA GEORG"/AU OR "VON SAMSON HIMMEL ST JERNA G"/AU OR "VON SAMSON HIMMELSRJEMA G"/AU OR "VON SAMSON HIMMELST JERNA G"/AU OR "VON SAMSON HIMMELSTJERNA A"/AU OR "VON SAMSON HIMMELSTJERNA G"/AU OR "VON SAMSON HIMMELSTJERNA GEORG"/AU)

=> s e23

L4 2 "VON SAMSONHIMMELSTJERNA G"/AU

=> s l1-l4

L5 256 (L1 OR L2 OR L3 OR L4)

=> s l5 and endoparasit?

L6 62 L5 AND ENDOPARASIT?

=> dup rem l6

PROCESSING COMPLETED FOR L6

L7 55 DUP REM L6 (7 DUPLICATES REMOVED)

=> s l7 and depositeptide

L8 0 L7 AND DEPOSITEPTIDE

=> s 17 and depsipeptide
L9 14 L7 AND DEPSIPEPTIDE

=> d bib ab 1-14

L9 ANSWER 1 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-629043 [68] WPIDS
DNC C2002-177712
TI Use of **depsipeptide** for control of **endoparasites**, e.g.
cestodes, trematodes, nematodes or acantocephalans, as solid in specific
crystal modification.
DC B03 C02
IN HARDER, A; KALBE, J; TRAEUBEL, M; VON SAMSON-HIMMELSTJERNA, G;
VON SAMSON-HIMMELSTJERNA, G
PA (FARB) BAYER AG
CYC 100
PI DE 10104362 A1 20020808 (200268)* 6p
WO 2002066048 A1 20020829 (200268) DE
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW
ADT DE 10104362 A1 DE 2001-10104362 20010201; WO 2002066048 A1 WO 2002-EP541
20020121
PRAI DE 2001-10104362 20010201
AB DE 10104362 A UPAB: 20021022
NOVELTY - Use of a specific **depsipeptide** (I), as a solid in
crystal modification I.
DETAILED DESCRIPTION - Use of a specific **depsipeptide** of
formula (I), as a solid in crystal modification I.
ACTIVITY - Antiparasitic.
Sheep were infected with 5000 L3 larvae of *Haemonchus contortus*, then
treated with 0.1 mg/kg (orally in a gelatine capsule) of (I) as crystal
modification I.
Anthelmintic activity, as measured from the number of worm eggs in
the feces, was over 95%. Similar doses of other crystal modifications were
less effective with activity 75% or lower.
MECHANISM OF ACTION - None given in the source material.
USE - (I) is used for control (treatment or prevention) of
endoparasites, e.g. cestodes, trematodes, nematodes or
acantocephalans, in humans and other animals (e.g. mammals, birds, fish,
reptiles or insects), and is active against all, or individual, stages of
the life cycle, of normally sensitive or resistant strains.
ADVANTAGE - Crystal modification I has greater bioavailability, and
thus activity, than other modifications.
Dwg.0/0

L9 ANSWER 2 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-076332 [11] WPIDS
DNC C2002-023023
TI Article for oral administration of veterinary drugs, especially
depsipeptide endoparasitocides, comprising
aroma-containing starch-based extrudate, is readily accepted by animals
such as dogs.
DC B03 C02
IN GEISSLER, K; HARDER, A; KALBE, J; TRAEUBEL, M; VON
SAMSON-HIMMELSTJERNA, G
PA (FARB) BAYER AG
CYC 97

PI DE 10031044 A1 20020103 (200211)* 11p
 WO 2002000202 A1 20020103 (200211) DE
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
 KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
 SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001079664 A 20020108 (200235)
 NO 2002006209 A 20030123 (200320)
 CZ 2002004141 A3 20030312 (200324)
 EP 1296655 A1 20030402 (200325) DE
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR
 BR 2001011914 A 20030513 (200335)
 KR 2003023874 A 20030320 (200346)
 ADT DE 10031044 A1 DE 2000-10031044 20000626; WO 2002000202 A1 WO 2001-EP6836
 20010618; AU 2001079664 A AU 2001-79664 20010618; NO 2002006209 A WO
 2001-EP6836 20010618, NO 2002-6209 20021223; CZ 2002004141 A3 WO
 2001-EP6836 20010618, CZ 2002-4141 20010618; EP 1296655 A1 EP 2001-957856
 20010618, WO 2001-EP6836 20010618; BR 2001011914 A BR 2001-11914 20010618,
 WO 2001-EP6836 20010618; KR 2003023874 A KR 2002-717197 20021217
 FDT AU 2001079664 A Based on WO 200200202; CZ 2002004141 A3 Based on WO
 200200202; EP 1296655 A1 Based on WO 200200202; BR 2001011914 A Based on
 WO 200200202
 PRAI DE 2000-10031044 20000626
 AB DE 10031044 A UPAB: 20020215
 NOVELTY - A starch-based extruded shaped article (A) contains special
 aromas, consistency-providing agents and veterinary drugs (I).
 DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the
 preparation of (A), by mixing the components and further processing at
 temperatures below 150 deg. C.
 USE - (A) is useful for the administration of oral administration of
 (I) to animals such as dogs, cats or horses. (I) are specifically cyclic
 depsipeptides (I'), consisting of aminoacid and hydroxycarboxylic acid
 units and having 6-30 ring or chain atoms (claimed). (I') are
endoparasitocides (for therapeutic or prophylactic use), described
 e.g. in EP382173, DE4317432, DE4317457 and DE4317458.
 ADVANTAGE - (A) is readily accepted by and palatable to animals.
 Addition of meat is unnecessary. (A) is readily prepared by conventional
 extrusion, and provides a simple method of administration of (I).
 Dwg.0/0

 L9 ANSWER 3 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
 AN 2001-523377 [58] WPIDS
 DNC C2001-156416
 TI **Endoparasiticide** composition effective on topical
 administration, comprises solution of **depsipeptide** in solvent
 such as 1,2-isopropylidene-glycerol.
 DC B03 C02
 IN HARDER, A; KALBE, J; MENCKE, N; STEGEMANN, M; TRAEUBEL, M; VON
SAMSON-HIMMELST JERNA, G; VON SAMSON-HIMMELSTJERNA, G;
 TRAUBEL, M; VON-SAMSON-HIMMELSTJERNA, G
 PA (FARB) BAYER AG; (HARD-I) HARDER A; (KALB-I) KALBE J; (MENC-I) MENCKE N;
 (STEG-I) STEGEMANN M; (TRAU-I) TRAUBEL M; (VONS-I) VON-SAMSON-
 HIMMELSTJERNA G
 CYC 95
 PI DE 10008128 A1 20010823 (200158)* 10p
 WO 2001062268 A1 20010830 (200158) DE
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001040605 A 20010903 (200202)

BR 2001008562 A 20021112 (200281)

NO 2002003976 A 20021021 (200281)

EP 1259250 A1 20021127 (200302) DE

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

CZ 2002002867 A3 20030115 (200309)

KR 2002072577 A 20020916 (200311)

HU 2002004554 A2 20030528 (200341)

CN 1404397 A 20030319 (200344)

US 2003125244 A1 20030703 (200345)

ADT DE 10008128 A1 DE 2000-10008128 20000222; WO 2001062268 A1 WO 2001-EP1392
20010209; AU 2001040605 A AU 2001-40605 20010209; BR 2001008562 A BR
2001-8562 20010209, WO 2001-EP1392 20010209; NO 2002003976 A WO
2001-EP1392 20010209, NO 2002-3976 20020821; EP 1259250 A1 EP 2001-911623
20010209, WO 2001-EP1392 20010209; CZ 2002002867 A3 WO 2001-EP1392
20010209, CZ 2002-2867 20010209; KR 2002072577 A KR 2002-710032 20020803;
HU 2002004554 A2 WO 2001-EP1392 20010209, HU 2002-4554 20010209; CN
1404397 A CN 2001-805400 20010209; US 2003125244 A1 WO 2001-EP1392
20010209, US 2002-204880 20020822

FDT AU 2001040605 A Based on WO 200162268; BR 2001008562 A Based on WO
200162268; EP 1259250 A1 Based on WO 200162268; CZ 2002002867 A3 Based on
WO 200162268; HU 2002004554 A2 Based on WO 200162268

PRAI DE 2000-10008128 20000222

AB DE 10008128 A UPAB: 20011010

NOVELTY - Composition (A) containing a cyclic **depsipeptide** (I)
(optionally together with other active agents) additionally contains at
least one solvent (II) and is formulated for topical administration to
animals.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the
preparation of (A), by mixing (I) with (II) and optionally further
additives.

ACTIVITY - Antiparasitic; anthelmintic.

A solution of 5 wt.% **depsipeptide** (unspecified) in 66.5 wt.
% isopropylidene glycerol and 28.5 wt. % benzyl alcohol gave 100% control
of *Toxocara canis* and *Ancylostoma caninum* in dogs and *Toxocara cati* in
cats within 2-4 days at a **depsipeptide** dosage of 5 mg/kg.

MECHANISM OF ACTION - None given.

USE - (A) are used as **endoparasiticides** (claimed). They are
useful for therapeutic or prophylactic control of a broad spectrum of
endoparasites (including cestodes, trematodes, nematodes and
acanthocephalae) in animals such as cats or dogs. Use in humans is also
possible.

ADVANTAGE - In the form of (A), (I) are highly effective on
topical/transdermal administration in controlling **endoparasites**
in the gastrointestinal tract, despite the fact that molecules (especially
peptides) of molecular weight more than 1000 usually show poor skin
penetration on topical administration. The preparations (A) also have good
long-term stability.

Dwg.0/0

L9 ANSWER 4 OF 14 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2001-041784 [06] WPIDS

DNC C2001-012205

TI Synergistic ectoparasiticide combination for use in human or veterinary
medicine, comprising cyclic **depsipeptide** and piperazine compound
as potentiating agent.

DC B03 C02

IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G

PA (FARB) BAYER AG

CYC 93

PI DE 19921887 A1 20001116 (200106)* 15p
 WO 2000069425 A2 20001123 (200106) DE
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000055237 A 20001205 (200113)
 BR 2000010499 A 20020213 (200220)
 NO 2001005398 A 20011105 (200222)
 SK 2001001626 A3 20020305 (200225)
 EP 1189615 A2 20020327 (200229) DE
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 KR 2001109527 A 20011210 (200237)
 CZ 2001004060 A3 20020612 (200251)
 CN 1352559 A 20020605 (200261)
 HU 2002001201 A2 20020828 (200264)
 ZA 2001008238 A 20021224 (200309) 51p
 JP 2002544224 W 20021224 (200313) 46p
 ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014
 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR
 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO
 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO
 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235
 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555
 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504;
 CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014
 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP
 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504
 FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO
 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on
 WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2
 Based on WO 200069425; JP 2002544224 W Based on WO 200069425
 PRAI DE 1999-19921887 19990512
 AB DE 19921887 A UPAB: 20021105
 NOVELTY - The use of piperazine derivatives (I) is claimed for
 potentiating the **endoparasitic** activity of cyclic depsipeptides
 (II), consisting of aminoacids and hydroxycarboxylic acids as ring
 components and having 24 ring atoms.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
 (i) **endoparasitic** compositions containing (I) and (II); and
 (ii) the use of (I) together with (II) for the preparation of
endoparasitic compositions.
 ACTIVITY - Anthelmintic.
 In tests against *Heterakis spumosa* in mice, piperazine (Ia) at 4 x
 250 mg/kg alone or '**depsipeptide** I' (IIa) (see WO9325543) at 4 x
 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at
 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm
 reduction.
 MECHANISM OF ACTION - None given.
 USE - The combinations of (I) and (II) are useful in human or
 veterinary medicine for controlling pathogenic **endoparasites**,
 specifically cestodes, trematodes, nematodes or acanthocephalae. Activity
 is demonstrated in tests against *Trichinella spiralis* in vitro and against
Heterakis spumosa or *Nematospiroides dibius* in mice.
 ADVANTAGE - The combination of (I) and (II) (both known
 ectoparasiticides) has synergistic action, due to potentiation of the
 activity of (II) by (I).
 Dwg.0/0

AN 1998-532765 [46] WPIDS
DNC C1998-159906
TI New cyclic thio-**depsipeptide(s)** - useful for controlling
endoparasites.
DC B04 C03
IN BONSE, G; HARDER, A; JESCHKE, P; LINUMA, K; MENCKE, N; SAKANAKA, O;
VON SAMSON-HIMMELSTJERNA, G; IINUMA, K; VON SAMSON, G;
VON SAMSON HIMMELSTJERNA, G; SAMSON-HIMMELSTJERNA, G V
PA (FARB) BAYER AG; (MEIJ) MEIJI SEIKA KAISHA LTD
CYC 82
PI DE 19713626 A1 19981008 (199846)* 26p
WO 9843965 A1 19981008 (199846) DE
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA
PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW
AU 9870388 A 19981022 (199910)
EP 973756 A1 20000126 (200010) DE
R: CH DE ES FR GB IT LI NL
CN 1259128 A 20000705 (200052)
NZ 338102 A 20010223 (200115)
AU 731789 B 20010405 (200125)
KR 2000076392 A 20001226 (200134)
US 6265537 B1 20010724 (200146)
JP 2001524952 W 20011204 (200203) 83p
EP 973756 B1 20030326 (200323) DE
R: CH DE ES FR GB IT LI NL
DE 59807652 G 20030430 (200330)
ADT DE 19713626 A1 DE 1997-19713626 19970402; WO 9843965 A1 WO 1998-EP1628
19980320; AU 9870388 A AU 1998-70388 19980320; EP 973756 A1 EP 1998-917025
19980320, WO 1998-EP1628 19980320; CN 1259128 A CN 1998-805729 19980320;
NZ 338102 A NZ 1998-338102 19980320, WO 1998-EP1628 19980320; AU 731789 B
AU 1998-70388 19980320; KR 2000076392 A WO 1998-EP1628 19980320, KR
1999-708495 19990917; US 6265537 B1 WO 1998-EP1628 19980320, US
1999-381946 19990927; JP 2001524952 W JP 1998-541108 19980320, WO
1998-EP1628 19980320; EP 973756 B1 EP 1998-917025 19980320, WO 1998-EP1628
19980320; DE 59807652 G DE 1998-507652 19980320, EP 1998-917025 19980320,
WO 1998-EP1628 19980320
FDT AU 9870388 A Based on WO 9843965; EP 973756 A1 Based on WO 9843965; NZ
338102 A Based on WO 9843965; AU 731789 B Previous Publ. AU 9870388, Based
on WO 9843965; KR 2000076392 A Based on WO 9843965; US 6265537 B1 Based on
WO 9843965; JP 2001524952 W Based on WO 9843965; EP 973756 B1 Based on WO
9843965; DE 59807652 G Based on EP 973756, Based on WO 9843965
PRAI DE 1997-19713626 19970402
AB DE 19713626 A UPAB: 19981118
Cyclic thiodepsipeptides of formula (I), their optical isomers and
racemates are new: where R1, R4, R7 and R10 = H or 1-4C alkyl; R2, R5, R8,
R11 = H or optionally substituted 1-8C alkyl, 2-8C alkenyl, 3-6C
cycloalkyl, (3-6C)cycloalkyl-(1-2C)alkyl, aryl-(1-2C)alkyl,
heteroaryl-(1-2C)alkyl, aryl or heteroaryl; or R10+R11 complete a 5- or
6-membered ring that is optionally interrupted by O, S, SO or SO2 and
optionally substituted; R3, R9 = H, 1-8C alkyl, aryl-(1-2C)alkyl or
(3-6C)cycloalkyl-(1-2C)alkyl; R6, R12 = H or optionally substituted 1-8C
alkyl, 2-8C alkenyl, 3-6C cycloalkyl, (3-6C)cycloalkyl-(1-2C)alkyl,
aryl-(1-2C)alkyl, heteroaryl-(1-2C)alkyl, aryl or heteroaryl; X1-X4 = O or
S, at least one being S.
USE - for controlling **endoparasites** that infest humans and
other animals, including cestodes, trematodes, nematodes and
acanthocephalids.
Dwg.0/0

L9 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1999:819404 CAPLUS
 DN 132:36040
 TI Synthesis of sulfonyl-substituted cyclooctadepsipeptides for use in
 combating **endoparasites**
 IN Scherkenbeck, Jurgen; Dyker, Hubert; Plant, Andrew; **Harder, Achim**
 ; **Von Samson Himmelstjerna, Georg**
 PA Bayer A.-G., Germany
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9967281	A1	19991229	WO 1999-EP4028	19990611
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19828047	A1	19991230	DE 1998-19828047	19980624
	CA 2332122	AA	19991229	CA 1999-2332122	19990611
	AU 9945114	A1	20000110	AU 1999-45114	19990611
	BR 9911574	A	20010320	BR 1999-11574	19990611
	EP 1090031	A1	20010411	EP 1999-927953	19990611
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	JP 2002518520	T2	20020625	JP 2000-555932	19990611
PRAI	DE 1998-19828047	A	19980624		
	WO 1999-EP4028	W	19990611		
OS	MARPAT 132:36040				
AB	The invention relates to new substituted cyclooctadepsipeptides [(I); R, R1 = SO2-A in 2- or 4-position; A = NR2R3; R2, R3 = (independently) H, (substituted)alkyl; m = 1 - 2; n = 0 - 2], a method for their prepn. and their use for fighting endoparasites , as well as drugs contg. them as active ingredients. Thus, depsipeptide PF 1022 was reacted with chlorosulfonic acid, and the product further reacted with substituted amines (no data), to give the desired products. In in vivo tests using sheep infected with H. contortus, eight test compds. all resulted in >95% redn. of infection at 0.05 mg/kg p.o.; against T. colubriformis, four test compds. resulted in >95% redn. of infection at 0.25 mg/kg p.o.				
RE.CNT	3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L9 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1997:51502 CAPLUS
 DN 126:84585
 TI **Endoparasitic** drug combination
 IN Mencke, Norbert; **Harder, Achim**; Jeschke, Peter; Helpap, Barbara
 PA Bayer A.-G., Germany
 SO Ger. Offen., 17 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19520275	A1	19961205	DE 1995-19520275	19950602

TW 469133	B	20011221	TW 1996-85105513	19960510
CA 2222680	AA	19961205	CA 1996-2222680	19960520
WO 9638165	A2	19961205	WO 1996-EP2170	19960520
WO 9638165	A3	19970109		
W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9659004	A1	19961218	AU 1996-59004	19960520
AU 703048	B2	19990311		
EP 828506	A2	19980318	EP 1996-916137	19960520
EP 828506	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
CN 1191489	A	19980826	CN 1996-195661	19960520
JP 11506438	T2	19990608	JP 1996-536146	19960520
BR 9608961	A	19990629	BR 1996-8961	19960520
CZ 287290	B6	20001011	CZ 1997-3825	19960520
AT 213645	E	20020315	AT 1996-916137	19960520
ES 2173284	T3	20021016	ES 1996-916137	19960520
PL 184848	B1	20021231	PL 1996-323595	19960520
IL 118518	A1	19981227	IL 1996-118518	19960531
US 6159932	A	20001212	US 1997-952356	19971119
NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI DE 1995-19520275	A	19950602		
WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585

AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a synergistic nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin Bla/B1b 0.1 mg/kg orally was 100% effective against *Nematospiroides dubius* infestation in mice.

L9 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:379698 CAPLUS

DN 125:59134

TI Aromatic sulfonylation, sulfenylation, thiocyanation, and phosphorylation of cyclic depsipeptides in preparation of **endoparasitocides**.

IN Scherkenbeck, Juergen; Plant, Andrew; Jeschke, Peter; **Harder, Achim**; Mencke, Norbert

PA Bayer A.-G., Germany

SO Ger. Offen., 15 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4437198	A1	19960425	DE 1994-4437198	19941018
	CA 2202751	AA	19960425	CA 1995-2202751	19951005
	WO 9611945	A2	19960425	WO 1995-EP3926	19951005
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, UA, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	AU 9538038	A1	19960506	AU 1995-38038	19951005
	AU 698898	B2	19981112		
	EP 787141	A2	19970806	EP 1995-935902	19951005
	EP 787141	B1	20000830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE					
	CN 1162961	A	19971022	CN 1995-195746	19951005
	BR 9509377	A	19971118	BR 1995-9377	19951005

HU 77019	A2	19980302	HU 1997-2045	19951005
HU 218569	B	20001028		
JP 10511341	T2	19981104	JP 1995-512897	19951005
AT 195952	E	20000915	AT 1995-935902	19951005
ES 2149378	T3	20001101	ES 1995-935902	19951005
US 5874530	A	19990223	US 1997-817279	19970410
FI 9701610	A	19970416	FI 1997-1610	19970416
PRAI DE 1994-4437198	A	19941018		
WO 1995-EP3926	W	19951005		

OS MARPAT 125:59134

AB Title processes are carried out on cyclic depsipeptides prepd. from .alpha.-hydroxycarboxylic acids and .alpha.-amino acids and contg. 6-24 ring atoms and .gtoreq.1 Ph ring using the appropriate reagents, optionally in the presence of catalysts, additives, and/or diluents. Cyclic depsipeptides [I; .gtoreq.1 of R3-R10 = sulfonylated, sulfenylated, thiocyanated, or phosphorylated Ph, PhCH2; R1, R2, R11, R12 = H, (substituted) alkyl, cycloalkyl, aralkyl, aryl; R3, R5, R7, R9 = H, (substituted) alkyl; R4, R6, R8, R10 = H, (substituted) alkyl, alkenyl, cycloalkyl, aryl, aralkyl], useful as **endoparasitocides**, are claimed. I (R1, R2, R5, R9, R11, R12 = Me; R4, R6, R8, R10 = CH2CHMe2; R3, R7 = morpholine-4-sulfonyl) was effective against Hemonchus contortus in sheep at 0.5 mg/kg.

L9 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:951170 CAPLUS

DN 124:9453

TI Preparation of cyclic depsipeptides as **endoparasitocides**

IN Scherkenbeck, Juergen; Jeschke, Peter; Plant, Andrew; **Harder, Achim**; Mencke, Norbert

PA Bayer A.-G., Germany

SO Ger. Offen., 31 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4401389	A1	19950720	DE 1994-4401389	19940119
	EP 664297	A1	19950726	EP 1995-100198	19950109
	EP 664297	B1	19980408		
	ES 2115269	T3	19980616	ES 1995-100198	19950109
	JP 07206897	A2	19950808	JP 1995-21325	19950113
	US 5663140	A	19970902	US 1995-372543	19950113
PRAI	DE 1994-4401389		19940119		

OS MARPAT 124:9453

AB Title compds. [I; R1,R4 = H, (cyclo)alkyl, (hetero)aryl(alkyl), etc.; R2,R3,R5,R6 = H, (un)substituted alkyl, alkenyl, (hetero)aryl(alkyl), etc.] were prepd. Thus, prepd. I (R1 = R3 = R4 = R6 = Me, R2 = R5 = CMe3) had ED of 10mg/kg orally and/or i.v. against Haemonchus contortus in sheep.

L9 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:913288 CAPLUS

DN 123:340963

TI Preparation of cyclic depsipeptides having 18 ring atoms as **endoparasitocides**.

IN Jeschke, Peter; Scherkenbeck, Juergen; Bonse, Gerhard; Bischoff, Erwin; Mencke, Norbert; **Harder, Achim**; Londershausen, Michael; Mueller, Hartwig

PA Bayer A.-G., Germany

SO Eur. Pat. Appl., 42 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 658551	A1	19950621	EP 1994-119130	19941205
	EP 658551	B1	19990519		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE				
	DE 4342907	A1	19950622	DE 1993-4342907	19931216
	AT 180254	E	19990615	AT 1994-119130	19941205
	ES 2133153	T3	19990901	ES 1994-119130	19941205
	JP 07196687	A2	19950801	JP 1994-331022	19941209
	US 5624897	A	19970429	US 1994-353409	19941209
	CA 2137961	AA	19950617	CA 1994-2137961	19941213
	AU 9480410	A1	19950622	AU 1994-80410	19941213
	AU 679585	B2	19970703		
	ZA 9410011	A	19950824	ZA 1994-10011	19941215

PRAI DE 1993-4342907 19931216

OS CASREACT 123:340963; MARPAT 123:340963

AB Title compds. [I; R = H, (cyclo)alkyl], were prepd. Thus, N-methylalanyl-D-lactyl-N-methylisoleucyl-D-lactyl-N-methyllleucyl-D-lactic acid (prepn. given) was stirred with (Me₂CH)₂NEt and bis(2-oxo-3-oxazolidinyl)phosphonic acid chloride in CH₂Cl₂ at 0.degree. to room temp. to give 59.8% title compd. (II). II was effective against Trichostrongylus colubriformis and Haemonchus contortus in sheep at 10 mg/kg orally or i.v.

L9 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1995:813210 CAPLUS

DN 124:53819

TI Cyclic depsipeptides containing lactic acid with 18 ring atoms as **endoparasitocidal** agents and process for their preparation

IN Jeschke, Peter; **Harder, Achim**; Mencke, Norbert; Kleinkauf, Horst; Zocher, Rainer

PA Bayer A.-G., Germany

SO Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 669343	A1	19950830	EP 1995-101909	19950213
	EP 669343	B1	20030115		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	DE 4406025	A1	19950831	DE 1994-4406025	19940224
	AT 231164	E	20030215	AT 1995-101909	19950213
	ES 2185671	T3	20030501	ES 1995-101909	19950213
	US 5656464	A	19970812	US 1995-390326	19950217
	CA 2143045	AA	19950825	CA 1995-2143045	19950221
	AU 9512387	A1	19950831	AU 1995-12387	19950221
	AU 689179	B2	19980326		
	JP 07252297	A2	19951003	JP 1995-55279	19950221
	FI 9500823	A	19950825	FI 1995-823	19950222
	NO 9500669	A	19950825	NO 1995-669	19950222
	PL 180162	B1	20001229	PL 1995-307415	19950222
	BR 9500757	A	19951024	BR 1995-757	19950223
	CN 1112932	A	19951206	CN 1995-102287	19950223
	ZA 9501524	A	19951208	ZA 1995-1524	19950223
	HU 72399	A2	19960429	HU 1995-555	19950223
	HU 219830	B	20010828		
	CZ 287506	B6	20001213	CZ 1995-482	19950223
	US 5945316	A	19990831	US 1997-821633	19970320
PRAI	DE 1994-4406025	A	19940224		

US 1995-390326 A3 19950217
 OS MARPAT 124:53819
 AB A process for the prodn. of optically active cyclic depsipeptides with 18 ring atoms by use of fungi of the genus *Fusarium* or their isolated enzyme preps. is claimed.

L9 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1995:763739 CAPLUS
 DN 123:179457
 TI **Endoparasitocidal** agents containing praziquantel or epsiprantel and cyclic depsipeptides
 IN Mencke, Norbert; **Harder, Achim**; Jeschke, Peter
 PA Bayer A.-G., Germany
 SO Eur. Pat. Appl., 39 pp.
 CODEN: EPXXDW
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 662326	A2	19950712	EP 1994-120772	19941227
	EP 662326	A3	19971217		
	EP 662326	B1	20011128		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	DE 4400464	A1	19950713	DE 1994-4400464	19940111
	AU 9481592	A1	19950720	AU 1994-81592	19941220
	AU 685535	B2	19980122		
	AT 209501	E	20011215	AT 1994-120772	19941227
	ES 2168285	T3	20020616	ES 1994-120772	19941227
	US 5589503	A	19961231	US 1995-368515	19950104
	FI 9500091	A	19950712	FI 1995-91	19950109
	JP 07223951	A2	19950822	JP 1995-16335	19950109
	IL 112285	A1	19990620	IL 1995-112285	19950109
	PL 180019	B1	20001229	PL 1995-306709	19950109
	NO 9500093	A	19950712	NO 1995-93	19950110
	HU 69180	A2	19950828	HU 1995-65	19950110
	ZA 9500136	A	19950907	ZA 1995-136	19950110
	CZ 290246	B6	20020612	CZ 1995-61	19950110
	CN 1121429	A	19960501	CN 1995-101158	19950111
	RU 2124364	C1	19990110	RU 1995-100759	19950111
PRAI	DE 1994-4400464	A	19940111		

OS MARPAT 123:179457
 AB Praziquantel and epsiprantel enhance the **endoparasitocidal** action of cyclic depsipeptides. Thus, a 1:1 combination of praziquantel and cyclo(N-methyl-L-leucyl-D-lactoyl-N-methyl-L-leucyl-D-.beta.-phenyllactoyl-N-methyl-L-leucyl-D-lactoyl-N-methyl-L-leucyl-D-.beta.-phenyllactoyl) (PF 1022) was 100% effective against exptl. infestation with *Ancylostoma caninum* in dogs. Syntheses of cyclic depsipeptides with 18 and 24 ring atoms and their linear precursors is described.

L9 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 1995:374823 CAPLUS
 DN 122:160697
 TI Preparation of octacyclodepsipeptides as **endoparasitocides**
 IN Scherckenbeck, Juergen; Jeschke, Peter; Lerchen, Hans-Georg; Hagemann, Hermann; **Harder, Achim**; Mencke, Norbert; Plant, Andrew
 PA Bayer A.-G., Germany
 SO Eur. Pat. Appl., 46 pp.
 CODEN: EPXXDW
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 626375	A1	19941130	EP 1994-107543	19940516
	EP 626375	B1	20020605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, SE				
	DE 4317457	A1	19941201	DE 1993-4317457	19930526
	AU 9460642	A1	19941201	AU 1994-60642	19940421
	AU 682847	B2	19971023		
	AT 218555	E	20020615	AT 1994-107543	19940516
	ES 2177555	T3	20021216	ES 1994-107543	19940516
	US 6369028	B1	20020409	US 1994-246029	19940519
	CA 2124059	AA	19941127	CA 1994-2124059	19940520
	JP 06340695	A2	19941213	JP 1994-129930	19940520
	ZA 9403638	A	19950126	ZA 1994-3638	19940525
	US 5777075	A	19980707	US 1995-510084	19950801
PRAI	DE 1993-4317457	A	19930526		
	US 1994-246029	A3	19940519		
OS	MARPAT 122:160697				
AB	Title compds. [I; R1, R2, R11, R12 = (cyclo)alkyl, haloalkyl, aryl(alkyl); R3, R5, R7, R9 = H, alkyl, aryl(alkyl), etc.; R4, R6, R8, R10 = H, alk(en)yl, aryl(alkyl), etc.] were prep'd. Thus, I (R1 = R2 = R5 = R9 = R11 = R12 = Me, R3 = R7 = CH2Ph, R4 = R6 = R8 = R10 = CHMe2) gave complete control of Haemonchus contortus in sheep at 5mg/kg orally.				

L9 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1994:606025 CAPLUS

DN 121:206025

TI Preparation of cyclic depsipeptides with 18 ring atoms as
endoparasitocides.

IN Jeschke, Peter; Scherckenbeck, Juergen; Bonse, Gerhard; Mencke, Norbert;
Harder, Achim; Londershausen, Michael; Bischoff, Erwin; Mueller,
Hartwig; Kurka, Peter

PA Bayer A.-G., Germany

SO Ger. Offen., 49 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	DE 4317458	A1	19931216	DE 1993-4317458	19930526
	WO 9325543	A2	19931223	WO 1993-EP1436	19930607
	WO 9325543	A3	19940526		
	W: AU, BR, BY, CA, CZ, HU, JP, KR, KZ, NZ, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9343236	A1	19940104	AU 1993-43236	19930607
	AU 668571	B2	19960509		
	EP 644883	A1	19950329	EP 1993-912908	19930607
	EP 644883	B1	19990915		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
	JP 07508723	T2	19950928	JP 1993-501102	19930607
	HU 73417	A2	19960729	HU 1994-3542	19930607
	AT 184598	E	19991015	AT 1993-912908	19930607
	ES 2137991	T3	20000101	ES 1993-912908	19930607
	CZ 286108	B6	20000112	CZ 1994-3106	19930607
	JP 3299752	B2	20020708	JP 1994-501102	19930607
	US 5821222	A	19981013	US 1996-728106	19961009
PRAI	DE 1992-4219157	A1	19920611		
	DE 1993-4317458	A	19930526		
	WO 1993-EP1436	A	19930607		
	US 1994-343517	B1	19941205		
OS	MARPAT 121:206025				
AB	Title compds. [I; R1, R3, R5 = alkyl, hydroxyalkyl, alkoxyalkyl, mercaptoalkyl, alkylsulfanylalkyl, aminoalkyl, carbamoylalkyl,				

guanidinoalkyl, alkenyl, cycloalkyl, (substituted) arylalkyl, etc.; R2, R4, R6 = alkyl, hydroxyalkyl, alkanoyloxyalkyl, alkoxyalkyl, aryloxyalkyl, alkylthioalkyl, carbamoylalkyl, aminoalkylsulfonyl, alkoxy-carbonylaminoalkyl, alkenyl, cycloalkyl, (substituted) aryl, arylalkyl, etc.), were prepd. Thus, Z-MeIle-D-Lac-OH (MeIle = N-methylisoleucyl, Lac = lactyl) was coupled with H-(MeIle-D-Lac)2OBu-t in CH2Cl2 using (Me2CH)2NEt/BOP-Cl to give 77.4% Z-(MeIle-D-Lac)3OBu-t, which was O-deprotected with HCl in CH2Cl2 (82.9%) followed by coupling with pentafluorophenol using DCC in EtOAc to give 54% Z-(MeIle-D-Lac)3OPfp. This in dioxane was added over 6 h to a mixt. of Pd/C, 4-pyrrolidinopyridine, and EtOH in dioxane at 95.degree. under H to give 36.8% title compd. II. II was effective against Haemonchus contortus in sheep at 5 mg/kg.

=> d his

(FILE 'HOME' ENTERED AT 15:41:55 ON 23 JUL 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003

E HARDER ACHIM/AU

L1 139 S E3
E VON SAMSON-HIMMELSTJERNA GEORG/AU
L2 2 S E4
E VON SAMSON GEORG/AU
L3 149 S E2-E12
L4 2 S E23
L5 256 S L1-L4
L6 62 S L5 AND ENDOPARASIT?
L7 55 DUP REM L6 (7 DUPLICATES REMOVED)
L8 0 S L7 AND DEPSIDEPTIDE
L9 14 S L7 AND DEPSIPEPTIDE

=> s l7 and piperazine

L10 1 L7 AND PIPERAZINE

=> d bib ab

L10 ANSWER 1 OF 1 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2001-041784 [06] WPIDS

DNC C2001-012205

TI Synergistic ectoparasiticide combination for use in human or veterinary medicine, comprising cyclic depsipeptide and **piperazine** compound as potentiating agent.

DC B03 C02

IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G

PA (FARB) BAYER AG

CYC 93

PI DE 19921887 A1 20001116 (200106)* 15p

WO 2000069425 A2 20001123 (200106) DE

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000055237 A 20001205 (200113)

BR 2000010499 A 20020213 (200220)

NO 2001005398 A 20011105 (200222)

SK 2001001626 A3 20020305 (200225)

EP 1189615 A2 20020327 (200229) DE

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI
 KR 2001109527 A 20011210 (200237)
 CZ 2001004060 A3 20020612 (200251)
 CN 1352559 A 20020605 (200261)
 HU 2002001201 A2 20020828 (200264)
 ZA 2001008238 A 20021224 (200309) 51p
 JP 2002544224 W 20021224 (200313) 46p
 ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014
 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR
 2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO
 2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO
 2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235
 20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555
 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504;
 CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014
 20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP
 2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504
 FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO
 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on
 WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2
 Based on WO 200069425; JP 2002544224 W Based on WO 200069425
 PRAI DE 1999-19921887 19990512
 AB DE 19921887 A UPAB: 20021105

NOVELTY - The use of **piperazine** derivatives (I) is claimed for
 potentiating the **endoparasitic** activity of cyclic depsipeptides
 (II), consisting of aminoacids and hydroxycarboxylic acids as ring
 components and having 24 ring atoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) **endoparasitic** compositions containing (I) and (II); and

(ii) the use of (I) together with (II) for the preparation of

endoparasitic compositions.

ACTIVITY - Anthelmintic.

In tests against *Heterakis spumosa* in mice, **piperazine** (Ia)
 at 4 x 250 mg/kg alone or 'depsipeptide I' (IIa) (see WO9325543) at 4 x 1
 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at 4
 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm
 reduction.

MECHANISM OF ACTION - None given.

USE - The combinations of (I) and (II) are useful in human or
 veterinary medicine for controlling pathogenic **endoparasites**,
 specifically cestodes, trematodes, nematodes or acanthocephalae. Activity
 is demonstrated in tests against *Trichinella spiralis* in vitro and against
Heterakis spumosa or *Nematospiroides dibius* in mice.

ADVANTAGE - The combination of (I) and (II) (both known
 ectoparasiticides) has synergistic action, due to potentiation of the
 activity of (II) by (I).

Dwg.0/0

=> s depsipeptide and piperazine

6 FILES SEARCHED...

L11 11 DEPSIPEPTIDE AND PIPERAZINE

=> dup rem l11

PROCESSING COMPLETED FOR L11

L12 7 DUP REM L11 (4 DUPLICATES REMOVED)

=> d bib ab 1-7

L12 ANSWER 1 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN

AN 2002064650 EMBASE

TI Isolation of a novel cyclic hexadepsipeptide pipalamycin from *Streptomyces*
 as an apoptosis-inducing agent.

AU Uchihata Y.; Ando N.; Ikeda Y.; Kondo S.; Hamada M.; Umezawa K.
 CS K. Umezawa, Department of Applied Chemistry, Faculty of Science and
 Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-0061,
 Japan. umezawa@applc.keio.ac.jp
 SO Journal of Antibiotics, (2002) 55/1 (1-5).
 Refs: 7
 ISSN: 0021-8820 CODEN: JANTAJ
 CY Japan
 DT Journal; Article
 FS 004 Microbiology
 016 Cancer
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 AB The novel cyclic hexadepsipeptide named pipalamycin was isolated from a
 culture filtrate of Streptomyces sp. ML297-90F8 as an apoptosis-inducing
 agent. The antibiotic was found to be consisting of each one mole of
 alanine, N-hydroxyalanine, glycine, N-acylated 3-hydroxyleucine, and two
 moles of piperazic acid. Pipalamycin induced apoptosis in
 apoptosis-resistant human pancreatic adenocarcinoma AsPC-1 cells at 0.3
 .mu.g/ml in 24-48 hours. It also showed antibacterial activity on
 Gram-positive bacteria such as Staphylococcus aureus and Micrococcus
 luteus. Fermentation, isolation, structural elucidation and the biological
 activities of pipalamycin are described.

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
 AN 2001:104442 CAPLUS
 DN 134:266216
 TI Morpholine-2,5-diones - their preparation and uses
 AU Vinsova, Jarmila
 CS Fac. Pharmacy, Charles Univ., Hradec Kralove, 500 05, Czech Rep.
 SO Chemicke Listy (2001), 95(1), 22-27
 CODEN: CHLSAC; ISSN: 0009-2770
 PB Ceska Spolecnost Chemicka
 DT Journal; General Review
 LA Czech
 AB Morpholine-2,5-diones are **depsipeptide** analogs of cyclic
 dipeptides, derivs. of **piperazine**-2,5-diones. In contrast to
 cyclodipeptides, which are formed by spontaneous cyclization, prepn. of
 cyclodidepsipeptides is not easy. Two main ways are used for cyclization
 of depsipeptides. Cyclization by the formation of ester bond seems more
 efficient than cyclization via the amide bond formation. The review with
 51 refs. deals briefly with all known methods of syntheses of
 morpholine-2,5-diones but attention is also paid to their biol. activity.
 They are of great interest for biomedical applications. Optically active
 morpholine-2,5-diones are used as monomers for synthesis of biodegradable
 polymers, as prodrugs of bioactive amino acids and, most recently, in drug
 delivery systems.

L12 ANSWER 3 OF 7 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STNDUPLICATE 1
 AN 2001-041784 [06] WPIDS
 DNC C2001-012205
 TI Synergistic ectoparasiticide combination for use in human or veterinary
 medicine, comprising cyclic **depsipeptide** and **piperazine**
 compound as potentiating agent.
 DC B03 C02
 IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G
 PA (FARB) BAYER AG
 CYC 93
 PI DE 19921887 A1 20001116 (200106)* 15p
 WO 2000069425 A2 20001123 (200106) DE
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000055237 A 20001205 (200113)

BR 2000010499 A 20020213 (200220)

NO 2001005398 A 20011105 (200222)

SK 2001001626 A3 20020305 (200225)

EP 1189615 A2 20020327 (200229) DE

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

KR 2001109527 A 20011210 (200237)

CZ 2001004060 A3 20020612 (200251)

CN 1352559 A 20020605 (200261)

HU 2002001201 A2 20020828 (200264)

ZA 2001008238 A 20021224 (200309) 51p

JP 2002544224 W 20021224 (200313) 46p

ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014
20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR
2000-10499 20000504, WO 2000-EP4014 20000504; NO 2001005398 A WO
2000-EP4014 20000504, NO 2001-5398 20011105; SK 2001001626 A3 WO
2000-EP4014 20000504, SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235
20000504, WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555
20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504, CZ 2001-4060 20000504;
CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014
20000504, HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP
2002544224 W JP 2000-617884 20000504, WO 2000-EP4014 20000504

FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO
200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on
WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2
Based on WO 200069425; JP 2002544224 W Based on WO 200069425

PRAI DE 1999-19921887 19990512

AB DE 19921887 A UPAB: 20021105

NOVELTY - The use of **piperazine** derivatives (I) is claimed for
potentiating the endoparasitic activity of cyclic depsipeptides (II),
consisting of aminoacids and hydroxycarboxylic acids as ring components
and having 24 ring atoms.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) endoparasitic compositions containing (I) and (II); and

(iii) the use of (I) together with (II) for the preparation of
endoparasitic compositions.

ACTIVITY - Anthelmintic.

In tests against *Heterakis spumosa* in mice, **piperazine** (Ia)
at 4 x 250 mg/kg alone or '**depsipeptide I**' (IIa) (see WO9325543)
at 4 x 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of
(Ia) at 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than
90%) worm reduction.

MECHANISM OF ACTION - None given.

USE - The combinations of (I) and (II) are useful in human or
veterinary medicine for controlling pathogenic endoparasites, specifically
cestodes, trematodes, nematodes or acanthocephalae. Activity is
demonstrated in tests against *Trichinella spiralis* in vitro and against
Heterakis spumosa or *Nematospiroides dibius* in mice.

ADVANTAGE - The combination of (I) and (II) (both known
ectoparasitocides) has synergistic action, due to potentiation of the
activity of (II) by (I).

Dwg.0/0

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:587076 CAPLUS

DN 133:193492

TI Preparation of cyclopeptides or cyclic depsipeptides as antifungal agents

IN Barrett, David; Tanaka, Akira; Okitsu, Osamu; Harada, Keiko; Ohki,
Hidenori; Yamanaka, Hideaki; Kawabata, Koji
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 300 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2000229998	A2	20000822	JP 1999-301639	19991022
PRAI	JP 1998-368524	A	19981208		
OS	MARPAT 133:193492				

AB The title compds. [I; R1 = H, alkyl, lower alkoxyalkyl, CO₂H, (un)substituted CONH₂, aryl, lower (ar)alkyl, or heterocyclic carbonyl; R2 = (un)protected CO₂H, (un)substituted heterocyclic carbonyl, (un)substituted NH₂, N+(R₅)₃.X-; wherein R₅ = (un)substituted lower alkyl or alkenyl; X = acid residue; R₁₁ = HO, (un)substituted lower alkoxy; R₁₂ = H, halo; R₁₃ = H, NO₂, NH₂, acylamino; or R₁₁ and R₁₃ are bonded together to form O-CONH or -O-C-CONH; R₁₄ = cyano, (un)substituted CONH₂, (un)protected lower aminoalkyl; Z = O, NH, alkyl-N; P = (CH₂)_n; n = 0,1], which inhibit the biosynthesis of .alpha.-1,3-glucan and are useful for the treatment or prevention of bacterial infection, e.g. pneumonia caused by *Pneumocystis carinii*, are prepd. Thus, I.HCl (R1 = tridecyl, R2-A = H₂N(CH₂)₃, R₁₁ = OH, R₁₂ = R₁₃ = H, R₁₄ = H₂NCO, P = CH₂, Z = O) was condensed with Et formimidate hydrochloride in the presence of diisopropylethylamine in DMF at room temp. for 4 days to give I.HCl [R2-A = NH:CHNH(CH₂)₃; R1, R2, R₁₁, R₁₂, R₁₃, R₁₄, P, Z = same as above] which showed min. inhibitory concn. of 0.20 .mu.g/mL against *Candida albicans* (FP633).

L12 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STM
DUPLICATE 2

AN 2001:32913 BIOSIS

DN PREV200100032913

TI Synergistic action of a cyclic **depsipeptide** and **piperazine** on nematodes.

AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz

CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany

SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.

ISSN: 0932-0113.

DT Article

LA English

SL English

AB The present study describes the synergistic effects of the cyclic **depsipeptide** BAY 44-4400 and **piperazine** in the treatment against the nematodes *Trichinella spiralis*, *Heligmosomoides polygyrus*, and *Heterakis spumosa*. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against *T. spiralis* larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of *H. polygyrus* worms from the intestine of infected mice, an additive effect was observed; **piperazine** alone exerted an efficacy of 54.4% and BAY 44-4400 alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of *H. spumosa* worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of BAY 44-4400 and **piperazine**. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve

chords of *H. spumosa* as compared with the single compounds.

L12 ANSWER 6 OF 7 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
AN 2000027028 EMBASE
TI Enantioselective synthesis of protected forms of (3R,5R)-5-hydroxypiperazic acid useful for synthesis.
AU Depew K.M.; Kamenecka T.M.; Danishefsky S.J.
CS K.M. Depew, Laboratory for Bioorganic Chemistry, Sloan-Kettering Inst. for Can. Res., 1275 York Avenue, New York, NY 10021, United States
SO Tetrahedron Letters, (15 Jan 2000) 41/3 (289-292).
Refs: 34
ISSN: 0040-4039 CODEN: TELEAY
PUI S 0040-4039(99)01958-9
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Protected versions of (3R,5R)-5-hydroxypiperazic acid were synthesized enantioselectively in two novel ways. The first derives its chirality from D- glutamic acid while the second uses an Evans amination and a diastereoselective bromolactonization to establish the two chiral centers. Given that this amino acid is a component of several depsipeptides, these two routes enable the synthesis of multigram quantities of protected versions of 2.

L12 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:364874 BIOSIS
DN PREV200000364874
TI The effect of the cyclic **depsipeptide** Bay 44-44 is synergistically enhanced by the GABA agonist **piperazine** - indicating a new neuropharmacological action.
AU von Samson-Himmelstjerna, G. (1); Nicolay, F.; Harder, A. (1); Mehlhorn, H.
CS (1) Bayer AG, Leverkusen Germany
SO European Journal of Neuroscience, (2000) Vol. 12, No. Supplement 11, pp. 43. print.
Meeting Info.: Meeting of the Federation of European Neuroscience Societies Brighton, UK June 24-28, 2000
ISSN: 0953-816X.
DT Conference
LA English
SL English

=> s endoparasit? and depsipeptide

L13 33 ENDOPARASIT? AND DEPSIPEPTIDE

=> s l13 and synerg?

L14 4 L13 AND SYNERG?

=> d bib ab 1-4

L14 ANSWER 1 OF 4 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2001-041784 [06] WPIDS
DNC C2001-012205
TI **Synergistic** ectoparasiticide combination for use in human or veterinary medicine, comprising cyclic **depsipeptide** and piperazine compound as potentiating agent.
DC B03 C02
IN HARDER, A; SAMSON-HIMMELSTJERNA, G; VON SAMSON-HIMMELSTJERNA, G
PA (FARB) BAYER AG
CYC 93

PI DE 19921887 A1 20001116 (200106)* 15p
 WO 2000069425 A2 20001123 (200106) DE
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000055237 A 20001205 (200113)
 BR 2000010499 A 20020213 (200220)
 NO 2001005398 A 20011105 (200222)
 SK 2001001626 A3 20020305 (200225)
 EP 1189615 A2 20020327 (200229) DE
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 KR 2001109527 A 20011210 (200237)
 CZ 2001004060 A3 20020612 (200251)
 CN 1352559 A 20020605 (200261)
 HU 2002001201 A2 20020828 (200264)
 ZA 2001008238 A 20021224 (200309) 51p
 JP 2002544224 W 20021224 (200313) 46p
 ADT DE 19921887 A1 DE 1999-19921887 19990512; WO 2000069425 A2 WO 2000-EP4014
 20000504; AU 2000055237 A AU 2000-55237 20000504; BR 2000010499 A BR
 2000-10499 20000504; WO 2000-EP4014 20000504; NO 2001005398 A WO
 2000-EP4014 20000504; NO 2001-5398 20011105; SK 2001001626 A3 WO
 2000-EP4014 20000504; SK 2001-1626 20000504; EP 1189615 A2 EP 2000-940235
 20000504; WO 2000-EP4014 20000504; KR 2001109527 A KR 2001-713555
 20011023; CZ 2001004060 A3 WO 2000-EP4014 20000504; CZ 2001-4060 20000504;
 CN 1352559 A CN 2000-807450 20000504; HU 2002001201 A2 WO 2000-EP4014
 20000504; HU 2002-1201 20000504; ZA 2001008238 A ZA 2001-8238 20011008; JP
 2002544224 W JP 2000-617884 20000504; WO 2000-EP4014 20000504
 FDT AU 2000055237 A Based on WO 200069425; BR 2000010499 A Based on WO
 200069425; SK 2001001626 A3 Based on WO 200069425; EP 1189615 A2 Based on
 WO 200069425; CZ 2001004060 A3 Based on WO 200069425; HU 2002001201 A2
 Based on WO 200069425; JP 2002544224 W Based on WO 200069425
 PRAI DE 1999-19921887 19990512
 AB DE 19921887 A UPAB: 20021105
 NOVELTY - The use of piperazine derivatives (I) is claimed for
 potentiating the **endoparasitic** activity of cyclic depsipeptides
 (II), consisting of aminoacids and hydroxycarboxylic acids as ring
 components and having 24 ring atoms.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
 (i) **endoparasitic** compositions containing (I) and (II); and
 (ii) the use of (I) together with (II) for the preparation of
endoparasitic compositions.
 ACTIVITY - Anthelmintic.
 In tests against *Heterakis spumosa* in mice, piperazine (Ia) at 4 x
 250 mg/kg alone or '**depsipeptide** I' (IIa) (see WO9325543) at 4 x
 1 mg/kg alone gave 50-75% worm reduction, whereas a combination of (Ia) at
 4 x 250 mg/kg and (IIa) at 4 x 1 mg/kg gave complete (more than 90%) worm
 reduction.
 MECHANISM OF ACTION - None given.
 USE - The combinations of (I) and (II) are useful in human or
 veterinary medicine for controlling pathogenic **endoparasites**,
 specifically cestodes, trematodes, nematodes or acanthocephalae. Activity
 is demonstrated in tests against *Trichinella spiralis* in vitro and against
Heterakis spumosa or *Nematospiroides dibius* in mice.
 ADVANTAGE - The combination of (I) and (II) (both known
 ectoparasiticides) has **synergistic** action, due to potentiation
 of the activity of (II) by (I).
 Dwg.0/0

AN 1997-034097 [03] WPIDS
 DNC C1997-010612
 TI **Synergistic** endo-parasitic agent, e.g. for treatment of domestic
 pets - contains macrocyclic lactone, e.g. avermectin, cyclic-
depsipeptide and opt. praziquantil or epsiprantel.
 DC B03 C02
 IN HARDER, A; HELPAP, B; JESCHKE, P; MENCKE, N; KOELBL, B
 PA (FARB) BAYER AG
 CYC 45
 PI WO 9638165 A2 19961205 (199703)* DE 35p
 RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL OA PT SE
 W: AU BB BG BR BY CA CN CZ HU JP KR KZ LK MX NO NZ PL RO RU SK TR UA
 US
 DE 19520275 A1 19961205 (199704) 18p
 WO 9638165 A3 19970109 (199713)
 AU 9659004 A 19961218 (199714)
 ZA 9604473 A 19970430 (199723) 35p
 NO 9705516 A 19980106 (199812)
 EP 828506 A2 19980318 (199815) DE
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
 CZ 9703825 A3 19980318 (199817)
 SK 9701599 A3 19980708 (199836)
 NZ 309073 A 19981223 (199906)
 IL 118518 A 19981227 (199907)
 AU 703048 B 19990311 (199922)
 HU 9900346 A2 19990628 (199931)
 JP 11506438 W 19990608 (199933) 39p
 BR 9608961 A 19990629 (199937)
 MX 9709245 A1 19980301 (200002)
 KR 99022094 A 19990325 (200023)
 CZ 287290 B6 20001011 (200060)
 US 6159932 A 20001212 (200067)
 EP 828506 B1 20020227 (200215) DE
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI NL PT SE
 DE 59608798 G 20020404 (200225)
 TW 469133 A 20011221 (200254)
 CN 1191489 A 19980826 (200275)
 ES 2173284 T3 20021016 (200279)
 ADT WO 9638165 A2 WO 1996-EP2170 19960520; DE 19520275 A1 DE 1995-19520275
 19950602; WO 9638165 A3 WO 1996-EP2170 19960520; AU 9659004 A AU
 1996-59004 19960520; ZA 9604473 A ZA 1996-4473 19960531; NO 9705516 A WO
 1996-EP2170 19960520, NO 1997-5516 19971201; EP 828506 A2 EP 1996-916137
 19960520, WO 1996-EP2170 19960520; CZ 9703825 A3 WO 1996-EP2170 19960520,
 CZ 1997-3825 19960520; SK 9701599 A3 WO 1996-EP2170 19960520, SK 1997-1599
 19960520; NZ 309073 A NZ 1996-309073 19960520, WO 1996-EP2170 19960520; IL
 118518 A IL 1996-118518 19960531; AU 703048 B AU 1996-59004 19960520; HU
 9900346 A2 WO 1996-EP2170 19960520, HU 1999-346 19960520; JP 11506438 W JP
 1996-536146 19960520, WO 1996-EP2170 19960520; BR 9608961 A BR 1996-8961
 19960520, WO 1996-EP2170 19960520; MX 9709245 A1 MX 1997-9245 19971128; KR
 99022094 A WO 1996-EP2170 19960520, KR 1997-708573 19971128; CZ 287290 B6
 WO 1996-EP2170 19960520, CZ 1997-3825 19960520; US 6159932 A WO
 1996-EP2170 19960520, US 1997-952356 19971119; EP 828506 B1 EP 1996-916137
 19960520, WO 1996-EP2170 19960520; DE 59608798 G DE 1996-508798 19960520,
 EP 1996-916137 19960520, WO 1996-EP2170 19960520; TW 469133 A TW
 1996-105513 19960510; CN 1191489 A CN 1996-195661 19960520; ES 2173284 T3
 EP 1996-916137 19960520
 FDT AU 9659004 A Based on WO 9638165; EP 828506 A2 Based on WO 9638165; CZ
 9703825 A3 Based on WO 9638165; NZ 309073 A Based on WO 9638165; AU 703048
 B Previous Publ. AU 9659004, Based on WO 9638165; HU 9900346 A2 Based on
 WO 9638165; JP 11506438 W Based on WO 9638165; BR 9608961 A Based on WO
 9638165; KR 99022094 A Based on WO 9638165; CZ 287290 B6 Previous Publ. CZ
 9703825, Based on WO 9638165; US 6159932 A Based on WO 9638165; EP 828506
 B1 Based on WO 9638165; DE 59608798 G Based on EP 828506, Based on WO

9638165; ES 2173284 T3 Based on EP 828506

PRAI DE 1995-19520275 19950602

AB WO 9638165 A UPAB: 19970212

Endoparasitic agent comprises: a) at least one avermectin, ivermectin (22,23-dihydro-avermectin B1) or milbemycin macrocyclic lactone; b) a cyclic **depsipeptide** comprising amino acid and hydroxycarboxylic acid units and contg. 6-30 ring atoms; and opt. c) praziquantil or epsiprantel.

USE - The agent is useful for the treatment and prophylaxis of **endoparasite** infestations caused by filaria, cestodes, trematodes, nematodes and acantocephales in human beings and animals, including birds, fish and insects, eg. bees and silkworms.

ADVANTAGE - (a) and (b) exert a **synergistic** effect, which results in economical and ecological benefits as a result of a lower dosage regimen. Further, the agent is more effective than prior art agents, esp. in the control of nematodes which affect dogs and cats, partic. *Dirofilaria immitis*.

Dwg.0/0

L14 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:807726 CAPLUS

DN 133:359221

TI Piperazines for enhancement of cyclic **depsipeptide endoparasiticides**

IN Harder, Achim; Von Samson-Himmelstjerna, Georg

PA Bayer A.-G., Germany

SO Ger. Offen., 16 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19921887	A1	20001116	DE 1999-19921887	19990512
	WO 2000069425	A2	20001123	WO 2000-EP4014	20000504
	WO 2000069425	A3	20010315		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	BR 2000010499	A	20020213	BR 2000-10499	20000504
	EP 1189615	A2	20020327	EP 2000-940235	20000504
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002544224	T2	20021224	JP 2000-617884	20000504
	NO 2001005398	A	20011105	NO 2001-5398	20011105
	HR 2001000918	A1	20030430	HR 2001-918	20011211
PRAI	DE 1999-19921887	A	19990512		
	WO 2000-EP4014	W	20000504		

AB The invention discloses the use of piperazines to increase the **endoparasiticidal** effect of cyclic depsipeptides (having amino acids and hydroxy acids as ring components and with 24 ring atoms) for **endoparasiticidal** medicaments.

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:51502 CAPLUS

DN 126:84585

TI **Endoparasitic** drug combination

IN Mencke, Norbert; Harder, Achim; Jeschke, Peter; Helpap, Barbara
 PA Bayer A.-G., Germany
 SO Ger. Offen., 17 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19520275	A1	19961205	DE 1995-19520275	19950602
	TW 469133	B	20011221	TW 1996-85105513	19960510
	CA 2222680	AA	19961205	CA 1996-2222680	19960520
	WO 9638165	A2	19961205	WO 1996-EP2170	19960520
	WO 9638165	A3	19970109		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659004	A1	19961218	AU 1996-59004	19960520
	AU 703048	B2	19990311		
	EP 828506	A2	19980318	EP 1996-916137	19960520
	EP 828506	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	CN 1191489	A	19980826	CN 1996-195661	19960520
	JP 11506438	T2	19990608	JP 1996-536146	19960520
	BR 9608961	A	19990629	BR 1996-8961	19960520
	CZ 287290	B6	20001011	CZ 1997-3825	19960520
	AT 213645	E	20020315	AT 1996-916137	19960520
	ES 2173284	T3	20021016	ES 1996-916137	19960520
	PL 184848	B1	20021231	PL 1996-323595	19960520
	IL 118518	A1	19981227	IL 1996-118518	19960531
	US 6159932	A	20001212	US 1997-952356	19971119
	NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI	DE 1995-19520275	A	19950602		
	WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585

AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a **synergistic** nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin B1a/B1b 0.1 mg/kg orally was 100% effective against Nematospirides dubius infestation in mice.

=> s parasit? and drug (5a) combin?
 L15 5459 PARASIT? AND DRUG (5A) COMBIN?

=> s l15 and synerg?
 L16 467 L15 AND SYNERG?

=> s l16 and (piperazine? or depsipeptid?
 UNMATCHED LEFT PARENTHESIS 'AND (PIPERAZINE'
 The number of right parentheses in a query must be equal to the number of left parentheses.

=> s l16 and (piperazine? or depsipeptid?)
 L17 6 L16 AND (PIPERAZINE? OR DEPSIPEPTID?)

=> dup rem l17
 PROCESSING COMPLETED FOR L17
 L18 5 DUP REM L17 (1 DUPLICATE REMOVED)

=> d bib ab 1-5

L18 ANSWER 1 OF 5 CABA COPYRIGHT 2003 CABI on STN
AN 2001:31654 CABA
DN 20003026922
TI **Synergistic** action of a cyclic **depsipeptide** and **piperazine** on nematodes
AU Nicolay, F.; Harder, A.; Samson-Himmelstjerna, G. von; Mehlhorn, H.; von Samson-Himmelstjerna, G.
CS Institute of Zoomorphology, Cell Biology and Parasitology, Heinrich-Heine-University Dusseldorf, Universitätsstrasse 1, 40225 Dusseldorf, Germany.
SO Parasitology Research, (2000) Vol. 86, No. 12, pp. 982-992. 17 ref. ISSN: 0932-0113
DT Journal
LA English
AB The **synergistic** effects of the cyclic **depsipeptide** BAY 44-4400 and **piperazine** in the treatment of *Trichinella spiralis*, *Heligmosomoides polygyrus* and *Heterakis spumosa* infections in mice were investigated. The in vitro anthelmintic activity of a combination of the 2 compounds (1.7 motility units) against *T. spiralis* larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of *H. polygyrus* worms from the intestine of infected mice, an additive effect was observed; **piperazine** and BAY 44-4400 alone exerted individual efficacies of 54.4 and 44.4%, respectively, whereas the combination of both compounds had an efficacy of 97.5%. With regard to the expulsion of *H. spumosa* worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the individual compounds, showing that there was a considerable potentiation of the actions of BAY 44-4400 and **piperazine**. The **drug combination** exerted a significantly higher degree of degenerative effects on the intestine and on the nerve cords of *H. spumosa*, compared with the individual compounds.

L18 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1998:147346 CAPLUS
DN 128:213381
TI Compositions and methods for treating infections using analogs of indolicidin
IN Fraser, Janet R.; West, Michael H. P.; Krieger, Timothy J.; Taylor, Robert; Erfle, Douglas
PA Micrologix Biotech, Inc., Can.; Fraser, Janet R.; West, Michael H. P.; Krieger, Timothy J.; Taylor, Robert; Erfle, Douglas
SO PCT Int. Appl., 130 pp. CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9807745	A2	19980226	WO 1997-US14779	19970821
	WO 9807745	A3	19980709		
	W: AL, AM, AT, AU, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9743279	A1	19980306	AU 1997-43279	19970821
	EP 925308	A2	19990630	EP 1997-941352	19970821

EP 925308 B1 20020605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

JP 2001500477 T2 20010116 JP 1998-510994 19970821
EP 1174439 A2 20020123 EP 2001-119148 19970821
EP 1174439 A3 20030326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

AT 218579 E 20020615 AT 1997-941352 19970821
ES 2178000 T3 20021216 ES 1997-941352 19970821

PRAI US 1996-24754P P 19960821
US 1997-34949P P 19970113
EP 1997-941352 A3 19970821
WO 1997-US14779 W 19970821

OS MARPAT 128:213381

AB Compns. and methods for treating infections, esp. bacterial infections, are provided. Indolicidin peptide analogs contg. at least two basic amino acids are prepd. The analogs are administered as modified peptides, preferably contg. photo-oxidized solubilizer.

L18 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:51502 CAPLUS

DN 126:84585

TI Endoparasitic **drug combination**

IN Mencke, Norbert; Harder, Achim; Jeschke, Peter; Helpap, Barbara

PA Bayer A.-G., Germany

SO Ger. Offen., 17 pp.
CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19520275	A1	19961205	DE 1995-19520275	19950602
	TW 469133	B	20011221	TW 1996-85105513	19960510
	CA 2222680	AA	19961205	CA 1996-2222680	19960520
	WO 9638165	A2	19961205	WO 1996-EP2170	19960520
	WO 9638165	A3	19970109		
	W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9659004	A1	19961218	AU 1996-59004	19960520
	AU 703048	B2	19990311		
	EP 828506	A2	19980318	EP 1996-916137	19960520
	EP 828506	B1	20020227		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
	CN 1191489	A	19980826	CN 1996-195661	19960520
	JP 11506438	T2	19990608	JP 1996-536146	19960520
	BR 9608961	A	19990629	BR 1996-8961	19960520
	CZ 287290	B6	20001011	CZ 1997-3825	19960520
	AT 213645	E	20020315	AT 1996-916137	19960520
	ES 2173284	T3	20021016	ES 1996-916137	19960520
	PL 184848	B1	20021231	PL 1996-323595	19960520
	IL 118518	A1	19981227	IL 1996-118518	19960531
	US 6159932	A	20001212	US 1997-952356	19971119
	NO 9705516	A	19980106	NO 1997-5516	19971201
PRAI	DE 1995-19520275	A	19950602		
	WO 1996-EP2170	W	19960520		

OS MARPAT 126:84585

AB A combination of a macrocyclic lactone (avermectin, ivermectin, or milbemycin) with a cyclic **depsipeptide**, optionally including praziquantel or epsiprantel, is useful as a **synergistic**

nematocide for treatment of ascarid, hookworm, trichurid, and filarial infestations in mammals. Thus, a combination of PF 1022A (cyclic **depsipeptide**) 50.0 and ivermectin B1a/B1b 0.1 mg/kg orally was 100% effective against *Nematospiroides dubius* infestation in mice.

L18 ANSWER 4 OF 5 CABA COPYRIGHT 2003 CABI on STN
 AN 91:83681 CABA
 DN 912227873
 TI Efficacy of anthelmintics against mixed helminth infections in fowls
 AU Hadykto, M. V.; Kulik, O. M.
 CS Vsesoyuznyi Institut Vetpreparatov, Moscow, USSR.
 SO Veterinariya (Moskva), (1991) No. 3, pp. 43-46. 12 ref.
 ISSN: 0042-4846
 DT Journal
 LA Russian
 SL English
 AB In 200 hens carrying *Ascaridia galli* and *Heterakis gallinae*, the combined use of levamisole at 15 mg a head and **piperazine** at 150 mg a head, given on two consecutive days, had a **synergic** action. In 100 hens carying *Ascaridia galli* and unspecified cestodes, levamisole at 40 mg enhanced the cestocidal action of niclosamide at 200 mg a head.

L18 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 1
 AN 78122168 MEDLINE
 DN 78122168 PubMed ID: 629460
 TI Anthelmintic efficacy of thenium closylate-**piperazine** phosphate combination tablets against *Toxocara canis* in pups and young dogs.
 AU Corwin R M; Miller T A
 SO AMERICAN JOURNAL OF VETERINARY RESEARCH, (1978 Feb) 39 (2) 263-5.
 Journal code: 0375011. ISSN: 0002-9645.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 197804
 ED Entered STN: 19900314
 Last Updated on STN: 19900314
 Entered Medline: 19780426
 AB Thenum closylate-**piperazine** phosphate combination tablets, tablets containing either thenium or **piperazine**, and control tablets (excipients only) were administered in 2 doses 5 to 7.5 hours apart to weaned pups and young dogs, in critical controlled trials to test efficacy against naturally acquired infections of *Toxocara canis*. In the 1st trial, the combination tablets produced a mean clearance of 94% from 18 pups. Tablets containing thenium alone showed a mean clearance of 9% from 25 pups, and tablets containing **piperazine** alone caused a mean clearance of 56% from 16 pups. Clearances, corrected for spontaneous worm losses observed in pups treated with the control tablets, were 90% (combination), 5% (thenium alone), and 52% (**piperazine** alone). In the 2nd and 3rd trials, efficacy of the combination tablet in 15 pups was 78% when corrected for worm losses in pups which had received placebo (excipient) tablets. Each component in the combination tablet contributed its full single-entity efficacy and, if in combination, **synergistic** effect between the components.

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	ENTRY SESSION
FULL ESTIMATED COST	185.40 185.61
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE TOTAL
	ENTRY SESSION

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-9.77

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=> s bay 44-4400
L19 18 BAY 44-4400

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20 4 DUP REM L19 (14 DUPLICATES REMOVED)

=> d bib ab 1-4

L20 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

AN 2001:555185 BIOSIS

DN PREV200100555185

TI Filaricidal efficacy of anthelmintically active cyclodepsipeptides.

AU Zahner, Horst (1); Taubert, Anja; Harder, Achim; von Samson-Himmelstjerna,
Georg

CS (1) Institute for Parasitology, Justus Liebig University Giessen,
Rudolf-Buchheim-Strasse 2, D-35392, Giessen: horst.zahner@vetmed.uni-
giessen.de Germany

SO International Journal for Parasitology, (November, 2001) Vol. 31, No. 13,
pp. 1515-1522. print.
ISSN: 0020-7519.

DT Article

LA English

SL English

AB PF 1022A, a novel anthelmintically active cyclodepsipeptide, and
Bay 44-4400, a semisynthetic derivative of PF
1022A were tested for filaricidal efficacy in *Mastomys coucha* infected
with *Litomosoides sigmodontis*, *Acanthocheilonema viteae* and *Brugia malayi*.
The parent compound PF 1022A showed limited anti-filarial efficacy in L.

sigmodontis and *B. malayi* infected animals. Oral doses of 5X100 mg/kg on consecutive days caused only a temporary decrease of microfilariaemia levels. By contrast, **Bay 44-4400** was highly effective against microfilariae of all three species in single oral, subcutaneous and cutaneously applied (spot on) doses. Minimum effective doses (MED, reducing parasitaemia density by $\geq 95\%$) determined 3 and 7 days after treatment were 3.125-6.25 and 6.25-12.5 mg/kg, respectively. Using the spot on formulation, doses of 6.25 mg/kg (*L. sigmodontis*), 12.5 mg/kg (*A. viteae*) and 25 mg/kg (*B. malayi*) were required to cause reductions of microfilaraemia levels by $\geq 95\%$ until day 56. Adulticidal effects, determined as minimum curative doses (MCD, eliminating adult parasites within 56 days by $>95\%$) after single dose treatment were limited to *A. viteae* (MCD, 100 mg/kg independent of the route of administration). Repeated oral treatment (100 mg/kg on 5 consecutive days) killed all adult *L. sigmodontis* but did not affect *B. malayi*. However, single doses of 6.25 and 25 mg/kg resulted in severe pathological alterations of intrauterine stages of *L. sigmodontis* and *B. malayi*, respectively. These alterations may be responsible for long-lasting reductions of microfilaraemia even when curative effects could not be achieved.

- L20 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
- AN 2002:271147 BIOSIS
- DN PREV200200271147
- TI Activity of the cyclic depsipeptide emodepside (**BAY 44-4400**) against larval and adult stages of nematodes in rodents and the influence on worm survival.
- AU Harder, Achim (1); von Samson-Himmelstjerna, Georg
- CS (1) Business Group Animal Health, Research and Development, Biological Chemical Evaluation, Bayer AG, Alfred-Nobel-Strasse 50, 40789, Monheim: achim.harder.ah@bayer-ag.de Germany
- SO Parasitology Research, (November, 2001) Vol. 87, No. 11, pp. 924-928. print.
ISSN: 0932-0113.
- DT Article
- LA English
- AB The present investigations deal with the activity of the cyclic depsipeptide emodepside (**BAY 44-4400**) against larval and adult stages of three rodent nematodes. While emodepside acts strongly against the adult stages of the rat nematodes *Nippostrongylus brasiliensis* and *Strongyloides ratti*, as well as against the mouse nematode *Heligmosomoides polygyrus*, its actions against the larval stages of these nematodes vary according to the species. Thus, emodepside is highly effective against the lung and intestine larval stages of *N. brasiliensis* and *S. ratti*. By contrast, the larval stages of *H. polygyrus* in the intestine are only partly affected by higher emodepside dosages.
- L20 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
- AN 2001:478778 BIOSIS
- DN PREV200100478778
- TI Effects of **Bay 44-4400**, a new cyclodepsipeptide, on developing stages of filariae (*Acanthocheilonema viteae*, *Brugia malayi*, *Litomosoides sigmodontis*) in the rodent *Mastomys coucha*.
- AU Zahner, H. (1); Taubert, Anja; Harder, Achim; von Samson-Himmelstjerna, Georg
- CS (1) Institute of Parasitology, Justus Liebig University Giessen, Rudolf-Buchheim-Strasse 2, D-35392, Giessen: horst.zahner@vetmed.uni-giessen.de Germany
- SO Acta Tropica, (1 September, 2001) Vol. 80, No. 1, pp. 19-28. print.

ISSN: 0001-706X.

DT Article
LA English
SL English

AB **Bay 44-4400** was used as a spot on formulation and administered in single doses of 25 and 100 mg/kg to *Acanthocheilonema viteae*, *Brugia malayi*, and *Litomosoides sigmodontis* infected *Mastomys coucha* on various dates during prepatency, aiming to affect third stage larvae, fourth stage larvae or preadult worms. Microfilaraemia levels were controlled in comparison to untreated controls until necropsies were performed 100 days p.i. (*A. viteae*, *L. sigmodontis*) and 150 days p.i. (*B. malayi*) to determine the numbers of surviving worms and the condition of intrauterine developing stages. A significant proportion (86-100%) of larval and preadult stages of *A. viteae* were killed by **Bay 44-4400** at a dose of 100 mg/kg. A dose of 25 mg/kg had only insignificant effects on the developing parasites, however, it strongly reduced microfilaraemia levels caused by surviving worms in the early phase of patency. Larval and preadult *B. malayi* and *L. sigmodontis* were not killed by **Bay 44-4400** to a significant degree. Microfilaraemia developing by surviving parasites was generally and significantly reduced throughout the observation period when treatment was performed to affect the preadult parasites. In the other cases variable results were obtained. Intrauterine early embryonic stages were found to be pathologically altered in worms which had been treated at a preadult stage.

L20 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4

AN 2001:32913 BIOSIS

DN PREV200100032913

TI Synergistic action of a cyclic depsipeptide and piperazine on nematodes.

AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz

CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany

SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.

ISSN: 0932-0113.

DT Article
LA English
SL English

AB The present study describes the synergistic effects of the cyclic depsipeptide **BAY 44-4400** and piperazine in the treatment against the nematodes *Trichinella spiralis*, *Heligmosomoides polygyrus*, and *Heterakis spumosa*. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against *T. spiralis* larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of *H. polygyrus* worms from the intestine of infected mice, an additive effect was observed; piperazine alone exerted an efficacy of 54.4% and **BAY 44-4400** alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of *H. spumosa* worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of **BAY 44-4400** and piperazine. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve chords of *H. spumosa* as compared with the single compounds.

=> dhis

DHIS IS NOT A RECOGNIZED COMMAND

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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 15:41:55 ON 23 JUL 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
LIFESCI, CAPLUS' ENTERED AT 15:42:05 ON 23 JUL 2003

E HARDER ACHIM/AU

L1 139 S E3
E VON SAMSON-HIMMELSTJERNA GEORG/AU
L2 2 S E4
E VON SAMSON GEORG/AU
L3 149 S E2-E12
L4 2 S E23
L5 256 S L1-L4
L6 62 S L5 AND ENDOPARASIT?
L7 55 DUP REM L6 (7 DUPLICATES REMOVED)
L8 0 S L7 AND DEPSIDEPTIDE
L9 14 S L7 AND DEPSIPEPTIDE
L10 1 S L7 AND PIPERAZINE
L11 11 S DEPSIPEPTIDE AND PIPERAZINE
L12 7 DUP REM L11 (4 DUPLICATES REMOVED)
L13 33 S ENDOPARASIT? AND DEPSIPEPTIDE
L14 4 S L13 AND SYNERG?
L15 5459 S PARASIT? AND DRUG (5A) COMBIN?
L16 467 S L15 AND SYNERG?
L17 6 S L16 AND (PIPERAZINE? OR DEPSIPEPTID?)
L18 5 DUP REM L17 (1 DUPLICATE REMOVED)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
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L20 4 DUP REM L19 (14 DUPLICATES REMOVED)

=> s l19 and piperazine

L21 4 L19 AND PIPERAZINE

=> d ti 1-4

L21 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Synergistic action of a cyclic depsipeptide and **piperazine** on
nematodes.

L21 ANSWER 2 OF 4 MEDLINE on STN
TI Synergistic action of a cyclic depsipeptide and **piperazine** on
nematodes.

L21 ANSWER 3 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
TI Synergistic action of a cyclic depsipeptide and **piperazine** on
nematodes.

L21 ANSWER 4 OF 4 CABA COPYRIGHT 2003 CABI on STN
TI Synergistic action of a cyclic depsipeptide and **piperazine** on
nematodes.

=> d bib ab

L21 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2001:32913 BIOSIS

DN PREV200100032913
 TI Synergistic action of a cyclic depsipeptide and **piperazine** on nematodes.
 AU Nicolay, Frank; Harder, Achim (1); von Samson-Himmelstjerna, Georg; Mehlhorn, Heinz
 CS (1) Business Group Animal Health, Research and Development, Bayer AG, 51368, Leverkusen: achim.harder.ah@bayer-ag.de Germany
 SO Parasitology Research, (December, 2000) Vol. 86, No. 12, pp. 982-992. print.
 ISSN: 0932-0113.
 DT Article
 LA English
 SL English
 AB The present study describes the synergistic effects of the cyclic depsipeptide **BAY 44-4400** and **piperazine** in the treatment against the nematodes *Trichinella spiralis*, *Heligmosomoides polygyrus*, and *Heterakis spumosa*. The in vitro anthelmintic activity of a combination of the two compounds (1.7 motility units) against *T. spiralis* larvae was significantly higher than the sum of the individual drug effects (1.3 motility units). With regard to the rate of expulsion of *H. polygyrus* worms from the intestine of infected mice, an additive effect was observed; **piperazine** alone exerted an efficacy of 54.4% and **BAY 44-4400** alone, one of 44.4%, whereas the combination of these compounds had an efficacy of 97.5%. With regard to the expulsion of *H. spumosa* worms, the effect of the combination was more than 5 orders of magnitude greater than the sum of the effects of the single compounds, i.e., there was a considerable potentiation of the actions of **BAY 44-4400** and **piperazine**. Moreover, the combination exerted a significantly higher degree of degenerative effects on the intestine and on the nerve chords of *H. spumosa* as compared with the single compounds.

=> s pf1022a

L22 135 PF1022A

=> s l22 and piperazine

L23 0 L22 AND PIPERAZINE

=> s l22 and synerg?

L24 2 L22 AND SYNERG?

=> d bib ab 1-2

L24 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
 AN 1992:430273 BIOSIS
 DN BA94:82398
 TI NEUROPHARMACOLOGICAL MECHANISM OF ACTION OF **PF1022A** AN ANTINEMATODE ANTHELMINTIC WITH A NEW STRUCTURE OF CYCLIC DEPSIPEPTIDE ON ANGIOSTRONGYLUS-CANTONENSIS AND ISOLATED FROG RECTUS.
 AU TERADA M
 CS DEP. PARASITOL., HAMAMATSU UNIV. SCH. MED., 3600 HANDA-CHO, HAMAMATSU 431-31, JPN.
 SO JPN J PARASITOL, (1992) 41 (2), 108-117.
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 AB Mechanism of action of **PF1022A** was studied neuropharmacologically. Against *Angiostrongylus cantonensis*, **PF1022A** inhibited the motility at such a low concentration as 10⁻¹³ g/ml, and paralyzed the worm at 10⁻¹²-10⁻⁶ g/ml. The paralysis by the drug at 10⁻¹² g/ml was partially antagonized by gabergic antagonists like picrotoxin and bicuculline, and completely reversed when

N-methylcytisine (N-MC) was added with gabergic antagonists. On the other hand, in the preparations paralyzed by PF1022A (10-10 g/ml), the spasmogenic effects of N-MC and eserine were kept inhibited even with gabergic antagonists, while those of pyrantel were not inhibited. Paralysis by PF1022A (10-12 g/ml) was antagonized by Ca²⁺ combined with gabergic antagonists. The reversed motility by Ca²⁺ was again paralyzed by the addition of PF1022A (10-10 g/ml). The guanidine (2.5 .times. 10⁻³ M)-induced twitch response in the isolated frog rectus with or without N-MC was inhibited PF1022A (10-6 g/ml), while contraction by pyrantel was not inhibited in the paralyzed preparation. From these results, it is suggested that PF1022A affects **neuropharmacologically** the nematode and the frog rectus. And in *A. cantonensis*, the inhibition is produced synergistically by **stimulating** the gabergic mechanism and inhibiting the cholinergic mechanism. As the drug is extremely less toxic against host animals, it is quite likely that PF1022A becomes **available** as a superior antinematode drug.

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TI Neuropharmacological mechanism of action of **PF1022A**, an antinematode anthelmintic with a new structure of cyclic depsipeptide, on *Angiostrongylus cantonensis* and isolated frog rectus

AU Terada, M.

CS Department of Parasitology, Hamamatsu University School of Medicine, 3600 Handa-cho, Hamamatsu 431-31, Japan.

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AB The mechanism of action of **PF1022A** was studied neuropharmacologically. **PF1022A** inhibited motility in *A. cantonensis* at a concentration of 10-13 g/ml, and paralysed the worm at 10-12-10-6 g/ml. Paralysis by the drug at 10-12 g/ml was partially antagonized by gabergic antagonists like picrotoxin and bicuculline, and completely reversed when N-methylcytisine (N-MC) was added with gabergic antagonists. However in the preparations paralysed by PF1022A (10-10 g/ml), the spasmogenic effects of N-MC and eserine were kept inhibited even with gabergic antagonists, while those of pyrantel were not inhibited. Paralysis by PF1022A (10-12 g/ml) was antagonized by Ca²⁺ combined with gabergic antagonists. The reversed motility by Ca²⁺ was again paralysed by the addition of PF1022A (10-10 g/ml). The guanidine (2.5 x 10⁻³ M)-induced twitch response in the isolated frog rectus with or without N-MC was inhibited by PF1022A (10-6 g/ml), while contraction by pyrantel was not inhibited in the paralysed preparation. It is suggested that PF1022A affects **neuropharmacologically** the nematode and the frog rectus, and in *A. cantonensis*, the inhibition is produced synergistically by **stimulating** the gabergic mechanism and inhibiting the cholinergic mechanism. As the drug has a low toxicity against host animals it is thought likely that PF1022A will **become** available as a superior antinematode drug.